REMARKS

Claims 1-11, 13-14, 17-18, 21, 24, and 26-27 are currently under consideration.

1. The Claims Comply With the Written Description Requirement

Claims 1-11, 13-14, 17-18, 21, 24, and 26-27 are rejected by the Examiner under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. According to the Examiner, the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

According to the Examiner, the claim amendment received on November 19, 2007 added the following text to independent claim 1: "wherein more than one protein, peptide, protein fragment, or peptide fragment binds to each defined location on the array," however, applicants failed to point out support for the claim amendment in the originally filed specification. Furthermore, the Examiner of record did not find support for the claim amendment in the originally filed specification (i.e. more than peptide, protein or peptide fragment bound to each class "area" of the array).

In Applicant's response to the Examiner's rejection, Applicant directed the Examiner's attention to paragraph 17 of the originally filed specification which states the following: "Accordingly, proteins and peptides are classified by the present invention based on their ability to be captured and retained by a specific binding molecule. A heterogeneous class of peptides or proteins will bind to specific binding molecule due to the presence of a motif common to all members of a particular class. The identity of the motif bound in each class of peptides is, therefore, a consequence of the binding specificity of the binding molecule that defines that class".

In response, the Examiner stated that the limitation of "wherein more than one protein, peptide, protein fragment, or peptide fragment binds to each defined location on the array" requires multiple binding events at each defined location on the array. Therefore, more than one "sample" must bind each "class" on the array and paragraph 17 does not provide support for this limitation. Further, the Examiner alleged that while Applicant does have support for multiple binding events, the requirement that every class on the array must have multiple binding partners in the sample is not supported by the disclosure in paragraph 17.

Applicant respectfully submits that, for reasons detailed below, the Examiner's view is mistaken and that the currently pending claims are fully supported by the specification and the priority document as filed.

First, by definition, an array is an ordered pattern of features (e.g. spots). Thus, for protein arrays, this translates into an ordered pattern of spots, where a unique protein is located within each spot. In the present case, the applicants have a specific antibody located within each spot. This definition of an array is supported by the following references attached herewith as Exhibits A-E: Jenkins & Pennington (2001) Proteomics 1, 13-29 (Exhibit A); Sreekumar & Chinnaiyan (2002) Curr Opin Mol Ther. 4(6):587-93 (Exhibit B); Templin et al (2002) Drug Discov Today. 7(15):815-22 (Exhibit C); MacBeath (2002) Nat Genet. 32 Suppl:526-32 (Exhibit D); and Sreekumar & Chinnaiyan (2002) Biotechniques. Suppl:46-53 (Exhibit E)[1]. Moreover, Applicant maintains that one of ordinary skill in the art would understand this definition of an array.

Further, as supported by the cited references (Exhibits A-E) and as outlined under "Generation of affinity arrays" (see specification, paragraph [0143]), an array is fabricated mainly by dispensing a certain volume (commonly in the 300 pL scale) of the antibody at a

certain concentration (a conc. of 1-3 mg/ml is given as an example in the present application). Assuming the molecular weight of the scFv to be 28 kDa, accordingly $6.4x10^9$ – $1.94x10^{10}$ molecules will be deposited per spot, i.e. per defined location on the array. The fact that numerous proteins are deposited per defined position on an array is supported by Exhibits A-E, each of which is published prior to the submission of the present application.

Therefore, each defined location (i.e. spot) on the array will be occupied with numerous copies of the same antibody. Thus, contrary to the Examiner's assertion, multiple binding events can and will take place at each defined location (i.e. spot) on the array, without the need for "more than one "sample."

In the present case, the invention has numerous copies of the same antibody per defined spot, and these molecules are capable of performing multiple binding events when the sample is added (e.g. a digested proteome) resulting in the binding of several heterogeneous peptides that share a common motif. Hence, Applicant submits that the specification provides unbiased support for the currently pending claims.

Finally, these points are in fact already outlined in the last paragraph in the section "Arrays" (see specification paragraph [0051]), where it is stated that "[E]ach spot in the array may bind on average 2, 4, 6, 8, 10, 20, 40, 60, 80, 100, 200, 400, 600, 800, 900, 1000, 15000, 2000 or more different types of proteins, peptides, or fragments thereof, each having the same motif."

In view of the forgoing, Applicants respectfully submit that the written description requirements have been satisfied under 35 U.S.C. § 112, first paragraph.

2. The Claims Are Not Obvious in View of Minden and Nelson or in View of Minden and Barry

[1] Applicant has ordered a copy of Exhibit E and will provide the Examiner with a copy of Exhibit E upon receipt.

Claims 1-11,13-14,17-18, 21, and 24-27 are rejected under 35 U.S.C. §103(a) as being unpatentable over Minden et al. WO 02/086081 A2 ("Minden") and Nelson et al. U.S. Patent 6,887,713 ("Nelson").

According to the Examiner, Minden teaches methods of identifying a protein via assigning (i.e. separating) binding reagents to designated locations on an array, detecting the binding patterns, and comparing the binding pattern to a reference set (i.e. characterizing; please refer to the abstract, paragraphs [0005-0012], [0028-0032], [0035-0044], [0072-0074], [0077], [00117], Figures 1-11, and Table 1). In addition, Minden is said to further teach (i) that the molecular weight or mass of the binding reagents can be determined and that spectrometry can be utilized; (ii) that more than one protein can have the same epitope thus the common epitopes (i.e. more than one) would bind to the same defined location; (iii) that the total protein content of a cell or tissue can be utilized as the protein mixture; (iv) that the protein mixture can be fragmented with various chemical or enzymatic methods including trypsin; (v) that trypsin cleavage forms a peptide or epitope (i.e. motif) with C-terminal lysine or arginine residues; (vi) that the peptides or epitopes (i.e. motifs) can be at least three amino acids in length and can have at least two variable amino acids; (vii) that arrays can have different binding molecules at spatially addressable locations which bind to different binding reagents; (viii) that the protein mixture may comprise all (i.e. at least 10% of the peptides) of the proteins and that the epitopes cover the binding mixture; (ix) that the array can have 2-100 different proteins; (x) that the binding reagents can be antibodies; (xi) that the proteins are compared to a reference set (i.e. characterizing; (xii) that the reference set can include prediction about binding based on the predicted digests of a protein mixture; (xiii) that various binding reagents can be compared to a reference set or to other binding reagents.

According to the Examiner, although Minden does not specifically teach determining the abundance of the proteins by the use of desorption mass spectrometry or collision induced dissociation mass spectrometry, for present claims 1, 24, and 26, Nelson teaches analyzing complex biological mixtures utilizing "lab-on-a-chip" (i.e. chip-based microarrays) and MALDI-TOF (i.e. combination of both desorption mass spectrometry and collision induced dissociation mass spectrometry) wherein the proteins are quantified (i.e. abundance), internal reference standards are utilized, and determining the amount (i.e. abundance) of the proteins. According to the Examiner, the claims would have been obvious because the substitution of one known element (i.e. mass spectrometry providing mass information only) for another (i.e. mass spectrometry providing both mass and abundance information; MALDI-TOF) would have yielded predictable results to one of ordinary skill in the art at the time of the invention and/or (b) the claim would have been obvious because a particular known technique (i.e. MALDI-TOF utilized to determine mass and abundance of proteins) was recognized as part of the ordinary capabilities of one skilled in the art. See *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007).

Claims 1-11, 13-14, 17-18, 21, 24, and 26-27 are rejected by the Examiner under 35 U.S.C.§ 103(a) as being unpatentable over Minden and Barry et al. WO 0225287 ("Barry"). Barry is said by the Examiner, to teach methods of determining the binding and mass of trypsin digested proteins including antibodies from a cell including phage or tissue sample immobilized on an array. According to the Examiner, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of identifying proteins taught by Minden with the MALDI-TOF analysis taught by Barry.

Applicant maintains that, for reasons detailed below, the present invention is not render obvious by Minden, Nelson or Barry, either alone or in combination.

First, Minden describes an invention that uses an array consisting of motif-specific binders to identify a protein by comparing the binding pattern to a set of reference patterns generated from known proteins. The central idea of the invention described in Minden is to apply the peptide mixture generated by digestion of a sample containing a single protein, not a mixture of proteins, with the aim of identifying that protein. Minden discusses protein mixtures in paragraphs [0035] and [0066] but not in the context of samples to be analysed using the described invention.

Nelson describes a method in which the analyte is captured on a surface prior to analysis by MALDI-TOF. The aim in Nelson is not to separate unknown, complex samples into well-defined sub-classes prior to analysis but to combine known and used sample preparation techniques (e.g. solid phase extraction) with mass spectrometry into an integrated device or procedure.

Applicants maintain that the present invention relates to a method for proteomic analysis of a heterogeneous sample of proteins, or protein or peptide fragments by *separating the sample into heterogeneous classes* at spaced apart locations on an array wherein no advanced knowledge of the identity of individual proteins in a protein sample is required in order to perform the method of the present invention. There is no reference in Minden to such a method, nor would such a method have been obvious from the description in Minden either alone, or in combination with the teachings of Nelson or Barry.

The analytical problem the present invention addresses, namely reduction of complexity in biological samples into sub-classes in a defined and controlled manner prior to analysis, is of major concern in large research areas such as proteomics. Prior to the filing of the present invention, there was no reference in the prior art, to the use of motif-specific binders to address this issue.

Furthermore, a person skilled in the art would normally avoid and argue against using affinity reagents (e.g. antibodies) that bind to heterogeneous proteins, peptides or peptide fragments (e.g. different proteins, peptides and peptide fragments displaying a shared motif) as mono-specific binding reagents (i.e. reagents that bind to only one protein, peptide or peptide fragment) are normally used. Hence, the present application take advantage of a feature normally not used and rather avoided.

In light of these remarks, Applicant respectfully requests that the obviousness rejections be withdrawn.

CONCLUSION

In view of the foregoing amendments and remarks, it is believed that the subject claims are in condition for allowance, which action is earnestly solicited. If, in the opinion of the Examiner, a telephone conference would expedite prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,

KENYON & KENYON LLP

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By: /Carmella L. Stephens/
Carmella L. Stephens
Reg. No. 41,328

KENYON & KENYON LLP
One Broadway
New York, NY 10004
Telephone No. (212) 425-7200
Facsimile No. (212) 425-5288
CUSTOMER NO. 26646